Electronic Drug Product Reporting for Human Drug Compounding Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

REVISED DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

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For questions regarding this draft document contact the CDER Registration and Listing Staff at edrls@fda.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

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Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
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Office of the Commissionner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Phone : 301-796-4830

U.S. Department of Health and Human Services
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I. INTRODUCTION

This revised draft guidance explains how facilities that elect to register with FDA as outsourcing facilities are to submit drug product reports, consistent with section 503B of the Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 353b).[2] Section 503B of the FD&C Act provides that a facility that elects to register with FDA as an outsourcing facility must report to FDA information about the drugs compounded at that outsourcing facility in the form and manner that FDA may "prescribe by regulation or guidance."[3] This guidance describes who must report and what information they must provide and explains that drug compounding reports must be submitted in structured product labeling (SPL) format using FDA's electronic submissions system.

This guidance is a revision of the FDA draft guidance *Interim Product Reporting for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act*. FDA has revised that draft guidance to explain that outsourcing facilities are to report on compounded drugs using FDA's updated electronic submissions system. This draft revision supersedes the draft guidance *Interim Product Reporting for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act*.

Because Congress gave FDA explicit statutory authority to establish binding requirements in guidance, this guidance, once finalized, will not be subject to the usual restrictions in FDA's good guidance practices (GGP) regulations (i.e., the requirements that guidances not establish legally enforceable responsibilities and that guidances prominently display a statement of the document's nonbinding effect).[4]

This guidance prescribes how facilities are to submit drug reports to FDA under section 503B of the FD&C Act. Once finalized, it will have binding effect pursuant to section 503B(b)(2)(B).

II. BACKGROUND

[1] This guidance was prepared by the Office of Compliance, Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

[2] Section 503B was added to the FD&C Act by the Drug Quality and Security Act (DQSA), Pub. Law No. 113-54, on November 27, 2013.

[3] See section 503B(b)(2)(B).

[4] See 21 CFR 10.115(d) & (i).

The DQSA added new section 503B to the FD&C Act. Under section 503B(b), a compounder can elect to become an outsourcing facility by registering with FDA and meeting the other requirements described in section 503B of the FD&C Act.[5] Outsourcing facilities are inspected by FDA on a risk-based schedule and must comply with other provisions of the FD&C Act, such as current good manufacturing practice (CGMP) requirements. Details on other requirements applicable to outsourcing facilities are the subject of separate guidance documents.[6]

A facility that elects to become an outsourcing facility must, at the time of initial registration and twice each year, in June and December, submit to FDA a report identifying the drugs compounded by the facility during the previous six-month period.[7] For each identified drug, the outsourcing facility must provide certain information, which is listed in section 503B(b)(2)(A)(ii).

III. SCOPE OF THIS GUIDANCE

This revised draft guidance addresses the provisions in the DQSA regarding the drug reporting requirements for registered outsourcing facilities. Separate guidance documents provide instructions on which facilities should register with FDA as outsourcing facilities and how to do so. FDA has modified its electronic submission system to accept the electronic reports for drugs compounded by registered outsourcing facilities in SPL format. In the draft guidance for industry on *Interim Product Reporting for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act,* FDA indicated that when the Agency has modified its electronic submission system to allow outsourcers to submit information electronically through an SPL file, FDA intends to issue a draft guidance describing the updated format for long-term use.

This revised draft guidance provides instructions for outsourcing facilities to report compounded drugs in SPL format using FDA's electronic submission system, and supersedes FDA's draft guidance for *Interim Product Reporting for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act*.

IV. SUBMITTING COMPOUNDED PRODUCT REPORTS

A. Who Must Report and What Must They Report

Upon initial registration as an outsourcing facility under section 503B and twice each year (in June and December), each registrant must submit a drug product report to FDA.[8] This report

[5] See the guidance for industry *Registration for Human Drug Compounding Outsourcing Facilities under Section 503B of the FD&C Act*.

[6] All FDA guidances are available on the FDA guidance web page. FDA updates guidances regularly. To make sure you have the most recent version of a guidance, always consult the guidance web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

[7] Section 503B(b)(2) of the FD&C Act.

[8] Section 503B(b)(2)(A) of the FD&C Act.

must identify all drugs compounded at the outsourcing facility during the previous six-month period and provide all of the following information for each compounded drug:

- The active ingredient and strength of active ingredient per unit
- The source of the active ingredient (bulk or finished drug)
- The National Drug Code (NDC) number of the source drug or bulk active ingredient, if available
- The dosage form and route of administration
- The package description
- The number of individual units produced
- The NDC number of the final product, if assigned[9]

For purposes of drug product reporting under section 503B(b), the *strength of the active ingredient per unit* is the strength of the active ingredient per dose of the product.

The *package description* refers to the description of the smallest individual saleable package of the product for distribution and should include the type of package (e.g., vial, syringe, bottle) and the volume per package (e.g., 100 ml vial, 5 ml syringe, 100 tablets per bottle).

The *number of individual units produced* refers to the number of the smallest individual saleable packages of product for distribution.

For example, if a registered outsourcing facility compounds one thousand 100 ml vials of 5 mg/ml of Drug X, the *strength of the active ingredient per unit* is "5 mg/ml," the *package description* is "100 ml vials," and the *number of individual units produced* is "1,000 vials." Similarly, if a registered outsourcing facility compounds 5 mg tablets of Drug Y in one thousand bottles of 100 tablets each, the *strength of the active ingredient per unit* is "5 mg," the *package description* is "bottles of 100 tablets," and the *number of individual units produced* is "1,000 bottles."

B. When to Report

Registered outsourcing facilities must submit a report upon initial registration under section 503B of the FD&C Act and twice each year thereafter, once in June and once in December.[10] Drug product reports submitted between June 1 and June 30 of each year must report products produced during the previous six month period from December 1 through May 31. Reports submitted between December 1 and December 31 of each of year must report drug products produced during the previous six month period from June 1 through November 30.

C. How to Report

Section 503B(b)(3) of the FD&C Act requires outsourcing facilities to submit drug reporting information by electronic means, unless FDA grants a request for a waiver of such requirement

[9] Section 503B(b)(2)(A)(ii) of the FD&C Act.

[10] Section 503B(b)(2)(A) of the FD&C Act.

"because use of electronic means is not reasonable for the person requesting the waiver." FDA has modified its electronic submission system to accept electronic reports for drugs compounded by registered outsourcing facilities in SPL format. Therefore, a facility that elects to register with FDA as an outsourcing facility must submit drug product reporting information using FDA's electronic reporting system and the SPL format, unless FDA has granted the facility a waiver.

FDA has created a new SPL document type category for outsourcing facilities to submit drug product reports. Outsourcing facilities should submit drug product reporting information using the document type "Human Compounded Drug Label."[11] Section IV of the guidance for industry *Providing Regulatory Submissions in Electronic Format — Drug Establishment Registration and Drug Listing* provides detailed instructions on how to submit information using SPL. FDA also offers tools and information for creating and submitting SPL files. Additional information can be found at www.fda.gov/edrls.

FDA does not anticipate many instances in which electronic submission of reporting information will not be reasonable for a facility because the electronic system for submitting the information is an internet-based system accessible to all facilities seeking to register. It is likely to be easier to report product information electronically than in paper form. However, to apply for a waiver from the requirement to electronically submit drug reporting information, please provide a written request with a complete explanation of why the use of electronic means is not reasonable to the following:

> Drug Registration and Listing System Team
> U.S. Food and Drug Administration
> 10903 New Hampshire Avenue
> Silver Spring, MD 20993
>
> or
>
> Email: edrls@fda.hhs.gov

If you are granted a waiver, you will be instructed on how to submit product reporting information.

D. Confidentiality of Reporting Information

Section 503B(b)(2)(C) specifies that reports submitted under section 503B(b)(2) are exempt from inspection unless the Secretary finds that such an exemption would be inconsistent with the protection of the public health.

[11] The SPL document type name "Human Compounded Drug Label" was chosen by the FDA Data Standards Council to distinguish drug product reporting submissions under section 503B from drug registration and listing submissions under section 510.